UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,273	12/12/2001	Alasdair Mark Naylor	PC22013AADO	7030

7590 01/07/2005

Gregg C. Benson
Pfizer Inc.
Patent Department, MS4159
Eastern Point Road
Groton, CT 06340

EXAMINER	
HUI, SAN MING R	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 01/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/017,273	NAYLOR ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-9,11,13-25 and 28-44* is/are pending in the application.

4a) Of the above claim(s) *11,17-23,25,28-32 and 39-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-9,13-16,24,33-38 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation-in-part of 09/895,367, filed June 29, 2001, which claims benefit of 60/265,358, filed 1/31/2001. This application is a continuation-in-part of 09/905,846, filed July 13, 2001, which claims benefit of 60/291,722, filed may 17, 2001.

The subject matter of the instant application is not disclosed in the 09/895,367. 09/895,367 only discloses the use of NPY inhibitor with NEP inhibitors for treating male erectile dysfunction. However, 09/895,367 does not disclose the method of how to screen the appropriate NPY inhibitors or NPY1 inhibitors in the treatment of male erectile dysfunction.

This application also claims benefit of United Kingdom 0030647.2, filed December 15, 2000; United Kingdom 0108730.3, filed April 6, 2001; United Kingdom 0109910.0 filed April 23, 2001. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 8, 2004 has been entered.

Claims 3-9,11,13-25 and 28-44 are pending. Claims 11,17-23, 25, 28-32, and 39-43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11.

The filing of drawings filed May 29, 2002 and December 12, 2001 is acknowledged.

The outstanding rejection under 35 USC 112, second paragraph with regard to limitation "substantially no" in claim 4 is withdrawn in view of the amendments filed October 8, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-9,13-16,24,33-38 and 44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for B1BP3226, does not reasonably provide enablement for other NPY inhibitors that are selective for an NPY receptor associated with male genitalia. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In the instant case, the specification fails to provide information that would allow the skilled artisan to practice

the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that define "NPY inhibitors that are selective for an NPY receptor associated with male genitalia". Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only one "NPY inhibitors that are selective for an NPY receptor associated with male genitalia" examples is set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. There is no structural, chemical, or physical characteristics disclosed in relation to the selectivity of the NPY receptors associated with male genitalia in the instant specification. In fact, the

structures of NPY inhibitors examples disclosed in the specification are so diverse, it is unclear how to identify the appropriate NPY inhibitors that are selective for an NPY receptor associated with male genitalia. Without sufficient guidance or information, every compound known to man would be a potential candidate for practicing the instant invention. Therefore, one of skilled in the art would require individually assessing each embodiment for its physiological activity in order to practice the full scope of the invention. The instant claims are so broad that they read on all "NPY inhibitors that are selective for an NPY receptor associated with male genitalia", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Furthermore, applicant uses functional language, "NPY inhibitors that are selective for an NPY receptor associated with male genitalia" to define what the invention would be. Attention is directed to *General Electric Company v. Wabash Appliance Corporation et al* 37 USPQ 466 (US 1938), at 469, speaking to functional language at the point of novelty as herein employed: "the vice of a functional claim exists not only when a claims is "wholly" functional, if that is ever true, but when the inventor is painstaking when he recites what has already been seen, and then uses conveniently functional language at the exact point of novelty". Functional language at the point of novelty, as herein employed by Applicants, is further admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997) at 1406: stating this usage does "little more than outlin[e] goals appellants hope the recited

invention achieves and the problems the invention will hopefully ameliorate". Applicants functional language at the point of novelty fails to meet the requirements set forth under 35 USC 112, first paragraph. Claims employing functional language at the point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limits of the monopoly asserted" *General Electric Company v. Wabash Appliance Corporation et* supra, at 468. Claims thus constructed provide no guidance as to medicaments employed, levels for providing therapeutic benefit, or provide notice for those practicing in the art, limits of protection. Simply stated, the presented claims are an invitation to experiment, not reciting a specific medicament regimen useful for practicing the instant invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-9, 13-16, 24, 33-38, and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "NPYi when in use is selective for an NPY receptor associated with male genitalia" recited in claim 13 renders the claims indefinite. It is not clear what NPY is considered as associated with male genitalia. Therefore, it is not clear what NPY inhibitors are encompassed by the claims.

The expression "NPYi that is capable of selectively increasing the intracavernosal pressure" in claim 15 renders the claim indefinite as to what NPY inhibitors are encompassed by the claims. What NPY inhibitors are considered as NP inhibitors that selectively "increase the intracavernosal pressure"? And what NPY inhibitors will not selectively "increase the intracavernosal pressure"? In other words, the metes and bounds of the claim are not defined.

Response to the arguments

Applicant's arguments filed October 8, 2004 averring the amendments clarifies the claims have been considered, but are not found persuasive. It is not clear what NYP inhibitor compounds would be encompassed by the claims. The claims are merely describing the compounds functionally. The specification only discloses how to identify them but not what they are. There is no structural correlation with the NPY modulating activity disclosed. In other words, what moiety or functional groups are responsible for the selectivity of the herein claimed NPY receptors? Thus, the metes and bounds of the claims cannot be ascertained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3-9, 13-16, 24, 33, and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hutchison et al. (WO 98/03492) and Gregor et al. (WO 98/07420).

Hutchison et al. teaches a new class of neuropeptide Y1 specific ligands. Hutchison et al. also teaches a method of treating disorders associated with an inappropriate stimulation of neuropeptide Y receptors, including diseases related to sexual dysfunction and reproductive disorders, and abnormal drink and food intake such a obesity, anorexia, bulimia, and metabolic disorders (See page 9, lines 6-9 and 26-28 in particular). Hutchison et al. teaches the composition comprising the Neuropeptide Y1 antagonist is useful for oral, topical, parenteral administration (See page 11, lines 3-4).

Gregor et al. teaches compound F50 of the instant application as regulators of NPY activity (See page 15 and abstract in particular). Gregor et al. further teaches that the compound is useful as feeding suppressant (See page 19, lines 3-5) Gregor et al. further teaches that these compositions, which possess vasodilating activities and are capable of beneficially affecting the reperfusion of ischemic organs, can be administered orally, topically and locally (See page 19, lines 3-5 and 11-20, in particular).

The references do not expressly teach the neuropeptide inhibitors can increase the intracavernosal pressure. The references do not teach the herein claimed timing of dosing (.e., before or during sexual arousal).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the neuropeptide Y inhibitors of Hutchison et al. or Gregor et al. in a method of treating MED by increasing the intracavernosal pressure.

One of ordinary skill in the art would have been motivated to the neuropeptide Y inhibitors of Hutchison et al. or Gregor et al. in a method of treating MED by increasing the intracavernosal pressure because the neuropeptide Y inhibitors of Hutchison et al. or Gregor et al. are known to be useful as increase the blood flow perfusion. Increasing blood perfusion in the male genitalia would cause the increase of intracavernosal pressure and thereby erection. Examiner notes that F50 is the exemplified neuropeptide Y inhibitors and therefore considered as possessing the herein claimed characteristics (i.e., selective in NPY associated or located with male genitalia, having no, or substantially no, activity towards endopeptidase NEP and/or angiotensin converting enzyme of NPY inhibitor).

One of ordinary skill in the art would have been motivated to administer the NPY inhibitors of Hutchison and Gregor in the treatment of MED before or during sexual arousal. Optimization of dosage regimen is considered as within the purview of skilled artisan.

Response to arguments

Applicant's arguments filed October 8, 2004 averring the cited prior art's failure to provide motivation to combine the teachings of the cited references have been fully considered but they are not persuasive. Applicant further argues that the cited prior art teaches the increased blood flow to the penis but fails to teach the restricted blood flow out of the penis. These arguments have been considered, but are not found persuasive. As the applicant stated in the response, NPY played an important role in penile vein that causes the vein to be constricted. Therefore, logically NPY inhibitors would inhibit the constriction process and relax the vein, which in turn should increase the outflow of blood out of the penis and result in flaccid state of the penis. However, there is also teaching with regard to the distribution of neuropeptide Y nerve fibers that is concentrated in human penial arteries in the state of the art (See Wespes et al., the abstract). Since NPY is responsible for vasoconstriction, it would be logical to conclude, based on the teachings of the cited prior art, that the inhibition of NPY would lead to relaxation of blood vessel in both arteries and veins (more so in arteries than viens since the highest density of NPY fiber nerves are concentrated around the intracarvernous and dorsal arteries. Furthermore, the cited prior arts, clearly teaches the inhibition of NPY would lead to reperfusion of ischemic organs (See Gregor above). Therefore, employing an inhibitor of NPY would be reasonably expected to result in vasodilatation of intracarvenous arteries and veins, but more so in the arteries than vein, which leads to errection (See also the explanation below with regard to venous occlusion mechanism). Moreover, the applicant does not mention another mechanism

that would cause the occlusion of the vein. Erection occurs when the carvernosa arteries are relaxed by vasodilators, the blood flow to the penis increase. As the result, blood is trapped in the expanding sinusoidal system, which compresses the venules against the tunica albuginea, and causes venous occlusion. The increase in intracorporeal pressure leads tumescence and rigidity. The venous occlusion can be resulted directly from the mechanical compression of the expanding sinusoidal system and not form the activities of NPY (See Harrison's Principles of Internal Medicine, 13th ed., 1994, page 262-263, particularly page 262, col. 2, last paragraph). Thus, taking the cited prior arts together as a whole, one of ordinary skill in the art would be motivated to employ the vasodilatory NPY modulating compound of Gregor and Hutchison in a method of treating erectile dysfunction. In view of the explanation above, the claims are still properly rejected under 35 USC 103(a).

Applicant's arguments filed October 8, 2004 averring the cited prior art's failure to provide motivation have been considered, but are not found persuasive. The key issue of applicant's arguments is that neuropeptide Y, located in the dorsal vein of the penis, is responsible of vasoconstriction and therefore, the inhibition of NPY would lead to the increase outflow of blood and result in flaccidity. However, as discussed above, the cited prior art teaches that NPY fiber nerves are located in more abundant in intracavernous arteries than in veins. Therefore, in view of the cited prior arts, one of ordinary skill in the art would be reasonably expected the inhibition of NPY would lead to the relaxation of intracarvenous arteries and inflow of blood, which would leads to erection and venous occlusion (See explanation above).

Applicant's arguments filed October 8, 2004 averring the cited prior art's failure to provide motivation to select a NPY inhibitors have been considered, but are not found persuasive. This is not seen to be the basis of the rejection set forth in the previous office action. The cited prior art teaches the compound of Gregor and Hutchison as useful in treating sexual dysfunction and as vasodilators. Therefore, taking the teachings and the knowledge of the state of the art, one of ordinary skill in the art would employ these compounds in a method of treating erectile dysfunction.

Claims 34-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hutchison et al. and Viagra monograph, June 1999.

Hutchison et al. teaches a new class of neuropeptide Y1 specific ligands. Hutchison et al. also teaches a method of treating disorders associated with an inappropriate stimulation of neuropeptide Y receptors, including diseases related to sexual dysfunction and reproductive disorders, and abnormal drink and food intake such a obesity, anorexia, bulimia, and metabolic disorders (See page 9, lines 6-9 and 26-28 in particular). Hutchison et al. teaches the composition comprising the Neuropeptide Y1 antagonist is useful for oral, topical, parenteral administration (See page 11, lines 3-4).

Viagra monograph teaches Viagra is a PDE 5 inhibitors useful for treating erectile dysfunction and can be administered orally (See page 2381, col. 3, Clinical Pharmacology Section; page 2384, Dosage and Administration Section).

The references do not expressly teach to employ both NPY inhibitor and PDE 5 inhibitor together in a method of treating MED.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ both NPY inhibitor and PDE 5 inhibitor together in a method of treating MED.

One of ordinary skill in the art would have been motivated to employ both NPY inhibitor and PDE 5 inhibitor together in a method of treating MED. It is known in the art that both NPY inhibitor and PDE 5 inhibitor are useful in treating MED individually. Therefore, combining two agents, which are known to be useful to treat MED, individually into method useful for the very same purpose is *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069).

Response to arguments

Applicant's arguments filed October 8, 2004 averring the cited prior art's failure to provide motivation to combine the teachings of the cited prior arts have been considered, but are not found persuasive. The key issue of the applicant's arguments is that neuropeptide Y, located in the dorsal vein of the penis, is responsible of vasoconstriction and therefore, the inhibition of NPY would lead to the increase outflow of blood and result in flaccidity. However, as discussed above, the cited prior art teaches that NPY fiber nerves are located in more abundant in intracavernous arteries than in veins. Therefore, in view of the cited prior arts, one of ordinary skill in the art would be reasonably expected the inhibition of NPY would lead to the relaxation of intracarvenous arteries and inflow of blood, which would leads to erection and venous occlusion (See explanation above). Furthermore, PDE5 inhibitors such as sildenafil is

known to be useful for treating erectile dysfunction. Therefore, combining two agents, which are known to be useful to treat MED, individually into method useful for the very same purpose is *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Primary Examiner
Art Unit 1617